

c1 23. (amended) A method for *in vitro* screening for a cell whose phenotype is altered by expression of a transdominant intracellular bioactive peptide, said method comprising the steps:

a) introducing a molecular library comprising at least  $10^4$  different retroviral nucleic acid sequences, into a plurality of cells, wherein said retroviral nucleic acid sequences comprise an insertion of a nucleic acid sequence encoding a candidate bioactive peptide of from 4 to 100 amino acids in length, wherein said candidate bioactive peptide comprises a randomized portion biased to minimize stop codons, and wherein said retroviral nucleic acid sequences are expressed in said cells to produce a plurality of randomized peptides;

b) screening said plurality of cells to detect a cell exhibiting an altered phenotype due to the expression of a transdominant bioactive peptide.

24. (amended) A method for *in vitro* screening for a cell whose phenotype is altered by expression of a transdominant intracellular bioactive peptide, said method comprising the steps:

a) introducing a molecular library comprising at least  $10^4$  different retroviral nucleic acid sequences, into a plurality of cells, wherein said retroviral nucleic acid sequences comprise an insertion of a nucleic acid sequence encoding a candidate bioactive peptide of from 4 to 100 amino acids in length, wherein said candidate bioactive peptide comprises a randomized portion biased to interact with a class of molecules and wherein said retroviral nucleic acid sequences are expressed in said cells to produce a plurality of randomized peptides;

b) screening said plurality of cells to detect a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the expression of a transdominant bioactive peptide.

25. (amended) A method according to claim 23 or 24 further comprising the step:  
isolating said cell exhibiting an altered phenotype.

26. (amended) A method according to claim 25 further comprising the step:  
identifying said nucleic acid encoding said candidate bioactive peptide or identifying said candidate bioactive peptide.

c2 28. (amended) The method according to claim 23 wherein said randomized portion comprises codons having the sequence NNK, wherein N is selected from the group consisting of A, T, C and G, and K is selected from the group consisting of T and G.

C2  
Contd

29. (amended) The method according to claim 24 wherein said randomized portion biased to interact with a class of molecules comprises the sequence set forth in SEQ ID NO:47, XXXPPXPXX, wherein X is a randomized residue.

30. (amended) The method according to claim 23 or 24 wherein said candidate bioactive peptide is fused to a nucleic acid sequence encoding a presentation sequence capable of presenting said candidate bioactive peptide in a conformationally restricted form.

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C3

34. (amended) The method according to claim 23 or 24 wherein said library comprises at least  $10^5$  different retroviral nucleic acid sequences.

35. (amended) The method according to claim 23 or 24 wherein said library comprises at least  $10^6$  different retroviral nucleic acid sequences.

36. (amended) The method according to claim 23 or 24 wherein said library comprises at least  $10^7$  different retroviral nucleic acid sequences.

37. (amended) The method according to claim 23 or 24 wherein said library comprises at least  $10^8$  different retroviral nucleic acid sequences.

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C4

40. (amended) The method according to claim 23 or 24 wherein candidate bioactive peptide is fused to a nucleic acid sequence encoding a rescue sequence.

41. (amended) The method according to claim 23 or 24 wherein candidate bioactive peptide is fused to a nucleic acid sequence encoding a stability sequence.

42. (amended) The method according to claim 23 or 24 wherein candidate bioactive peptide is fused to a nucleic acid sequence encoding a dimerization sequence.

43. (amended) The method according to claim 23 or 24 wherein candidate bioactive peptide is fused to a nucleic acid sequence encoding a targeting sequence.

C4  
cont

44. (amended) The method according to claim 43 wherein said targeting sequence is selected from the group consisting of:

- a) a localizing signal sequence capable of constitutively localizing said candidate bioactive peptide to a predetermined subcellular locale;
  - b) a membrane-anchoring sequence capable of localizing said candidate bioactive peptide to a cellular membrane; and
  - c) a secretory signal sequence capable of effecting the secretion of said candidate bioactive peptide.
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C5

47. (amended) A molecular library of retroviruses comprising at least  $10^5$  different retroviral nucleic acid sequences wherein said retroviral nucleic acid sequences comprise an insertion of a nucleic acid sequence encoding a candidate bioactive peptide of from 4 to 100 amino acids in length, wherein said candidate bioactive peptide comprises a randomized portion biased to minimize stop codons.

48. (amended) The molecular library of retroviruses according to claim 47 comprising at least  $10^6$  different retroviral nucleic acid sequences.

49. (amended) The molecular library of retroviruses according to claim 47 comprising at least  $10^7$  different retroviral nucleic acid sequences.

50. (amended) The molecular library of retroviruses according to claim 47 comprising at least  $10^8$  different retroviral nucleic acid sequences.

51. (amended) A cellular library of mammalian cells containing a molecular library of retroviral constructs, said molecular library comprising at least  $10^5$  different retroviral nucleic acid sequences, wherein said retroviral nucleic acid sequences comprise an insertion of a nucleic acid sequence encoding a candidate bioactive peptide of from 4 to 100 amino acids in length, wherein said candidate bioactive peptide comprises a randomized portion biased to minimize stop codons.

52. (amended) The cellular library according to claim 51 wherein said constructs are integrated into the genome of said mammalian cells.

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